

DATA EVALUATION RECORD

STUDY 7b

CHEM 112600	Prohexadione calcium	§163-1
CAS No. 127277-53-6		
FORMULATION--00--ACTIVE INGREDIENT		

STUDY ID 44457789

O'Connor, J. 1992. BX-112: determination of the seepage behavior of BX-112 by soil column study in European soil (normal test). LSR Report No.: 91/0601. BASF Reg. Document No.: 92/11975. Unpublished study performed by Life Science Research Ltd., Suffolk, ENGLAND; and submitted by BASF Corporation, Research Triangle Park, NC.

DIRECT REVIEW TIME = 53 Hours

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CONCLUSIONS

Mobility - Leaching & Adsorption/Desorption

1. This study is not scientifically valid and not acceptable for the partial fulfillment of the data requirement for a soil mobility of prohexadione calcium (column leaching). Based on column leaching studies, cyclohexene ring-labeled [3,5-¹⁴C]prohexadione calcium, applied at a nominal concentration of 0.1 mg/kg, had a low mobility in the loam and loamy sand soil columns which were leached over a period of two days with 393 ml of distilled water. The test design and analytical method were inadequate to accurately determine the mobility of the test compound.
2. This study does not meet Subdivision N Guidelines for the partial fulfillment of EPA data requirements on soil mobility (column leaching) for the following reasons:
 - (i) the elution volume was not equivalent to 20 inches;
 - (ii) leaching solution was not 0.01-0.02 N CaCl₂ solution;
 - (iii) the soil treatment rate was not equal to the highest recommended rate for a single application;
 - (iv) leaching data for parent and residues were not reported adequately; and
 - (v) only foreign (two) soils were utilized in the study.
3. As an acid prohexadione is expected to show some mobility in soil. Prohexadione calcium mobility appears to be dependent on soil type and, under some environmental conditions, the chemical may leach down the soil profile. Although, this study does not provide acceptable data on parent and degradates movement in soil, the registrant submitted an acceptable adsorption/desorption study (MRID 4457787) and therefore the unaged soil column leaching study does not have to be repeated.

METHODOLOGY

Test Substance: Cyclohexene ring-labeled [3,5-¹⁴C]prohexadione calcium, calcium 3-oxido-4-propionyl-5-oxo-3-cyclohexene-carboxylate; radiochemical purity 98.8%, specific activity 3.62 Mbq/mg; Lot No. CP-1107.

Reference Substance: [¹⁴C]-atrazine, radiochemical purity no less than 99%, specific activity 4.28 Mbq/mg. KI-2817 (3,5-dioxo-4-propionyl-cyclohexane-1-carboxylic acid), purity 99.6%,

Lot No G15-04. KI-2790 (methyl 3,5-dioxo-4-propionyl-1-cyclohexane carboxylate), purity 100%, Lot No 3.

Soil Tested: Two European soils: the loam soil (Hallsworth, from England; 31% sand, 48% silt, 21% clay, 3.3% organic carbon, pH 5.8, CEC 26.4 meq/100 g) and the loamy sand soil (Newport, England; 80% sand, 12% silt, 8% clay, 0.6% organic carbon, pH 6.9, CEC 6.4 meq/100 g); stored at 4 °C. The study author classified the loam and the loamy sand soils (USDA classification) as a clay loam soil and a sandy loam soil, respectively (see attachment p. 17).

Test Design: Glass columns (5-cm i.d.) equipped with conical bottoms (filled with siliceous sand) were packed (while agitating) to a depth of 30 cm with sieved (2 mm; p. 116) loam soil and loamy sand soil; the columns were saturated with distilled water. The columns were treated (evenly over the surface) with cyclohexene ring-labeled [3,5-¹⁴C]prohexadione calcium, dissolved in distilled water, at a nominal concentration of 0.1 mg/kg (p. 22). Duplicate columns and control columns were utilized for each soil; four additional soil columns were treated with [¹⁴C]atrazine for comparison. CO₂ traps (1 M KOH and mono-ethanolamine:water, 20:80, v:v) were connected to the top of each column and to the leachate collection flasks (Figure 1, p. 46). The columns were leached with 393 mL distilled water over a 48-hour period (p. 23); leachate was collected in 100-mL fractions.

Aliquots of the leachate fractions (loam soil only) were analyzed for total radioactivity by LSC (p. 23); limits of detection and quantitation were not reported. Leachate fractions were placed in sealed glass containers connected to two CO₂ (0.1 M NaOH) traps in sequence. Fractions were acidified with 10 N sulfuric acid, aerated for 2 hours, and treated with nonradiolabeled parent. The fractions were extracted three times with chloroform; the method of extraction was unspecified. Duplicate aliquots of the organic and aqueous phases were analyzed for total radioactivity by LSC (p. 23).

The soil columns were divided into five 6-cm sections (p. 23). Each section was placed in a sealed glass container connected to two CO₂ (0.1 M NaOH) traps in sequence (p. 24). The soil samples were acidified with 1 N sulfuric acid and aerated for 17 hours. Samples were extracted by shaking with acetone and filtered. The combined filtrates were concentrated under vacuum and treated with nonradiolabeled parent. The filtrate was partitioned three times with chloroform. The organic and aqueous phases were brought to volume and duplicate aliquots were analyzed for total radioactivity by LSC. Duplicate subsamples of the post-extracted soil were analyzed for total radioactivity by LSC following combustion (p. 24).

To characterize [¹⁴C]residues, eluent and soil extracts containing >0.001 ppm were analyzed by TLC (p. 25). The soil extract (organic phase) was evaporated to dryness under vacuum at 40 °C and redissolved in chloroform, and an aliquot of nonradiolabeled parent was added (p. 24). The solution was evaporated to dryness, dissolved in methanol and analyzed using two-dimensional TLC on silica gel plates developed perpendicularly with benzene:methanol:acetic acid (45:8:4, v:v:v) followed by diisopropylether:formic acid:water (90:7:3, v:v:v). Samples were co-

chromatographed with nonradiolabeled reference standards and were visualized under UV (unspecified wavelength) light. Radioactive [^{14}C]residues were detected by linear analyzer. To confirm [^{14}C]residues were present as the parent compound or the methyl ester, a selected sample (loamy sand soil extract, 24- to 30-cm) was analyzed using one-dimensional TLC on silica gel plates developed with the first solvent system previously described (p. 26).

To confirm the presence of $^{14}\text{CO}_2$ in the KOH and NaOH traps, duplicate samples were precipitated with barium chloride and centrifuged; duplicate aliquots of supernatant were analyzed by LSC. The presence of $^{14}\text{CO}_2$ in the ethanolamine:water traps was not confirmed.

THE STUDY AUTHOR DATA SUMMARY

Table 1 and 2 (see attachment) present the total radioactivity distributions in the column soil sections, leachate (i.e., aqueous and organic extract, extracted eluent fraction), and traps, for the loamy sand and loam soil, respectively. Table 3 and 4 present the percent of radioactivity recovered in each soil segment of the BX-112 treated loamy sand soil (Table 3) and loam soil (Table 4), and atrazine columns. All data were reported with respect to depth of leaching; the top of the column was designated as 30 cm, while the bottom was designated as 0 cm. The results indicate that cyclohexene ring-labeled [3,5- ^{14}C]prohexadione calcium (radiochemical purity $\geq 98.8\%$), applied at a nominal concentration of 0.1 mg/kg, appeared to have a low mobility in the loam and loamy sand soil columns which were leached over a period of two days.

In both soil types the majority radioactivity remained near the surface (EFED notes that columns were not sufficiently eluted to promote soil movement effectively). More than half of the applied radioactivity was recovered as $^{14}\text{CO}_2$. Analysis of eluents and soil extracts with higher than 0.001 ppm concentrations revealed presence of KI-2817 as the only radiolabelled material. Radioactivity recoveries were 86.8% and 97.8% from the loamy sand and loam, respectively.

Loam soil

Based on LSC analysis, most of the total [^{14}C]residues retained in the soil column following leaching remained in the top 24- to 30-cm layer (Table 4). Total [^{14}C]residues in the 24- to 30-cm depth (top layer) were 32.8% and 32.4% of the applied radioactivity for the first and second columns, respectively. In the remaining layers and sand (bottom), $\leq 1.3\%$ of the applied radioactivity was present in both columns, respectively. Total [^{14}C]residues were present in the leachate (designated as wash) at 1.2% and 0.2% of the applied for the first and second columns, respectively. Radiolabeled $^{14}\text{CO}_2$ collected in the traps at the top of the column and in the leachate collection flasks accounted for means of 58.6% and 2.0% (reviewer-calculated) of the applied, respectively (Table 2). Radiolabeled $^{14}\text{CO}_2$ collected in the traps during leachate and soil extraction accounted for means of 0.11% (reviewer-calculated) and 0.6% of the applied radioactivity, respectively.

The material balance based on LSC analysis was 96.4-99.3% of the applied radioactivity for the two columns (Table 2).

Loamy sand soil

Most of the total [^{14}C]residues retained in the soil column following leaching remained in the top layer and decreased gradually down the column (Table 3). Total [^{14}C]residues in the 24- to 30-cm depth (top layer) were 9.8% and 7.5% of the applied radioactivity for the first and second columns, respectively. Total [^{14}C]residues were means of 5.9% at 18- to 24-cm (second layer from top), 4.3% at 12- to 18-cm, 2.5% at 6- to 12-cm, 1.3% at 0- to 6-cm and 1.0% in the sand (bottom). Total [^{14}C]residues in the leachate (designated as wash) were not determined (Table 3). Radiolabeled $^{14}\text{CO}_2$ collected in the traps at the top of the column and in the leachate collection flasks accounted for means of 41.9% and 8.8% (reviewer-calculated) of the applied, respectively (Table 1). Radiolabeled $^{14}\text{CO}_2$ collected in the traps during leachate and soil extraction accounted for means of 12.1% (reviewer-calculated) and 2.7% of the applied radioactivity, respectively.

Following column leaching, the material balance based on LSC analysis was 84.3-89.4% of the applied for the two columns (Table 1).

THE REVIEWERS' COMMENTS

1. This study is not scientifically valid and not acceptable for the partial fulfilment of the data requirement for soil mobility of prohexadione calcium (column leaching). Based on the depth of leaching prohexadione calcium, expressed only as total residues (parent compound plus degradates), had low mobility in the loam and loamy sand soil columns. The mobility determinations were of questionable validity. The test design and analytical method were inadequate to accurately determine the mobility of the test compound and its degradates for the following reasons:
 - A. The soil columns were not sufficiently eluted. The elution volume was ca. 8 inches (393 mL) while it was supposed to be equivalent to 20 inches which is 997 ml {i.e.; $((\pi * (\text{column diameter})^2)/4) * 20 \text{ inches} = (3.1416 * 5 * 5)/4 * 50.8 = 997 \text{ ml}$ }. Only a sufficient elution volume can provide downward movement of the parent and its degradates through the soil column.
 - B. The leaching solution was not 0.01-0.02 N CaCl_2 solution but distilled water. The use of distilled water could cause soil particles to disperse, decreasing the rate of infiltration and leaching. Additionally, the use of distilled water may lead to the removal of sorbed ions from soil particles, thereby affecting the degree of adsorption of the test material.

C. The soil treatment rate was not equal to the highest recommended rate for a single application. The fortification rate used in this study was equivalent to 0.1 ppm. Therefore, it was lower than the lowest proposed application rate. The lowest proposed application rate is 0.125 lb a.i./acre, applied three times per season, for peanuts and the highest is 0.825 lb a.i./acre, applied twice per season, for apples.

D. The analytical method may have been inadequate to characterize residues. The study author stated that a confirmation that the recovered radioactivity was present as the parent compound was not possible using the method of analysis supplied, as this involves the conversion of any parent present to 3,5-dioxo-4-propionyl-cyclohexane-1-carboxylic acid (KI-2817), which is also a metabolite in the degradation pathway (p. 33). The study author further stated that TLC analysis of the organo-soluble extracts identified KI-2817 as the only radiolabeled compound in the column present at >0.001 ppm.

E. The study author stated that storage in methanol led to the methylation of the parent acid to its methyl ester (KI-2817), which was found during the leaching analysis. Because the conditions that led to the transformation were artificially produced, the author stated that this did not affect the study (p. 31).

F. The bulk densities of the packed soils were not reported. Soil bulk densities should be measured and reported, and should be similar for all columns (hand packed) of the same soil.

G. All data were reported incorrectly with respect to depth of leaching. The top of the column was designated as 30 cm, while the bottom was designated as 0 cm. Generally, "0" indicates the top of the column and the values (cm) increase with depth.

H. Only foreign (two) soils were utilized for the unaged column leaching study. The EPA will accept foreign soils for two out of four soils required if the soils are classified according to the USDA soil taxonomic system and if they are representative of the soils in the typical use patterns for which the data are being submitted. The soil tested in this study may be not representative of the soils in the typical peanuts/apple growing areas of the United States. The study author classified the loam and the loamy sand soils (USDA particle-size classification) as a clay loam soil and a sandy loam soil, respectively (p. 17). The reviewer could not confirm that the soils were classified according to the USDA soil taxonomic classification system. A clarification by the study author is necessary. Additionally, soil names are required. The study author did not specify whether one of the soils utilized was the same type of soil used in an aerobic soil metabolism study. The reviewer noted that an aerobic metabolism study (MRID

44457785) utilizing a sandy loam soil from Holly Springs, NC was submitted. This sandy loam soil was used in a batch equilibrium study as well (MRID 44457787; p. 12).

I. The material balances (based on LSC analysis) of the loamy sand soil columns following column leaching were questionable (<90%); recoveries were 84.3% and 89.4% of the applied for the first and second columns, respectively (Table 1, p. 36). The study author stated that the lower recoveries could be accounted for by the loss of radioactivity (as $^{14}\text{CO}_2$) during analysis of the less strongly adsorbing system (p. 34).

J. Limits of detection and quantitation were not reported. The study author stated only that the limit of detection was derived statistically from background counts (p. 20). It is necessary that both limits of detection and quantitation be reported to allow the reviewer to evaluate the adequacy of the method.

2. Since prohexadione is an acid, it is expected to show some mobility in soil. Reviewed data indicate that prohexadione calcium mobility appears to be dependent on soil type and under some environmental conditions the chemical may leach down the soil profile. The linearized K_{dl} values were 0.50, 2.8, 9.1, and 11.0, for the sand soil (0.5% OM), the clay soil (3.1% OM), the loamy sand soil (1.1% OM), and the loam soil (4.5% OM), respectively (MRID 44457787).

Prohexadione Calcium

DER MRID 44457789

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Pages 8 through 23 are not included.

The material not included contains the following type of information:

- ☐ Identity of product inert ingredients.
- ☐ Identity of product impurities.
- ☐ Description of the product manufacturing process.
- ☐ Description of quality control procedures.
- ☐ Identity of the source of product ingredients.
- ☐ Sales or other commercial/financial information.
- ☐ A draft product label.
- ☐ The product confidential statement of formula.
- ☐ Information about a pending registration action.
- ☒ FIFRA registration data.
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The information not included is generally considered confidential by product registrants. If you have any questions, please contact the individual who prepared the response to your request.